REMARKS

I. Status of the claims

Claims 1-3 (canceled)

Claims 4-11 (withdrawn)

Claims 12-22 (currently amended)

Claims 12-22 are pending.

II. Specification is Amended to Correct Informalities

The embedded hyperlinks are amended and are replaced with a brief description wherever appropriate.

On page 2 of the Action, the examiner objected to the Appendix A being unnumbered and to the embedded hyperlinks in the specification. The Appendix A is amended to include page numbers and a CD-ROM version is attached herein.

III. The Examiner Did Not Establish a Prima Facie Showing of Lack of Utility Under 35 U.S.C. § 101

The examiner rejected claims 12-22 under 35 U.S.C. § 101 for lacking utility.

> To properly reject a claimed invention under 35 U.S.C. 101, the Office **must** (A) make a prima facie showing that the claimed invention lacks utility, and (B) **provide a sufficient evidentiary basis for factual assumptions** relied upon in establishing the *prima facie* showing. In *re Gaubert*, 524 F.2d 1222, 1224, 187 USPQ 664, 666 (CCPA 1975) ("Accordingly, the PTO must do **more than merely question operability** - it must set forth factual reasons which would lead one skilled in the art to question the objective truth of the statement of operability.").
>
> If the Office cannot develop a proper prima facie case and provide evidentiary support for a rejection under 35 U.S.C. 101, a rejection on this ground should not be imposed. See, *e.g.*, In *re Oetiker*, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992). (*emphasis added*). MPEP 2107.02

The present disclosure relates a collection of genes or partial segments that are expressed at moderate to high levels in primate hematopoietic tissue such as, for example CD34+ cells from bone marrow. The disclosure also compared the expression ratio of these gene in humans and non-human primate baboons. Several applications are disclosed in the application and some of these include determining whether a stem cell graft would successfully expand *ex vivo* and translating experimental results from primates to humans based on the gene expression levels on

a solid microchip. The data in Tables 1-3 and the Appendix A, demonstrate a practical application of the microarray with the collection of genes disclosed herein. The aforementioned applications meet the utility requirements under 35 U.S.C. § 101.

Furthermore, according to MPEP 2107.02:

> The prima facie showing must be set forth in a well-reasoned statement. Any rejection based on lack of utility should include a **detailed explanation** why the claimed invention has no specific and substantial credible utility. Whenever possible, the examiner **should provide documentary evidence** regardless of publication date (*e.g.*, scientific or technical journals, excerpts from treatises or books, or U.S. or foreign patents) to support the factual basis for the prima facie showing of no specific and substantial credible utility. (*emphasis added*).

The examiner based the rejections merely on his opinion and did not offer any evidentiary support as to why a skilled artisan would question the utilities disclosed in the application. On page 6 of the Action, the examiner mentions "data mining" does not have a "real world" use. Applicants disagree and emphasize that "data mining" is an important step in genomics to identify novel genes involved in a specific process such as, for example, hematopoiesis. The database disclosed in the present application relates a list of genes whose expression levels are moderate to high in hematopoietic tissue from humans and baboons. This collection represents a specific set of genes that are expressed to significant levels in both humans and baboons. The following is a partial list of instances where specific applications are disclosed in the specification:

Location in the specification	**Remarks**
Page 3, lines 20-25	To discover new genes involved in hematopoiesis and stem cell growth such as cell surface markers, growth factors, and receptors.
Page 4, lines 19-31; Page 5, lines 16-20	To determine if a transplanted tissue will engraft and to determine the effects of treatment by comparing the expression levels of genes in a microchip.
Page 5, lines 20-27	Direct correlation of experimental results after a treatment in baboons to humans based on gene expression levels.
Page 10, lines 25-32	Example 1: Use of the Hematopoetic Database of the Present Invention to Expand a Stem Cell Graft Ex Vivo

IV. Claims 12-22 Are Amended

Support for the claim amendments can be found at least in the following instances in the specification:

Claim Terms	Suport
majority of the DNA molecules	Page 3, lines 30-32: "relates to a database that is a dataset which specifies the majority of genes expressed"
expression analysis	Page 5, lines 17-20: "The expression of genes on the chip would be compared to that level of expression" Page 7, lines 27-30 : "Comparison of the hybridization profiles of the human and baboon marrow made it possible to determine that both had similar expression patterns for the majority of genes."
cdna id, GenBank accession numbers, acc	Support can be found in the Appendix A header that specifies the cdna id, and GenBank acc numbers.
comparing expression levels of the DNA molecules in the transplant and a host	Page 10, lines 27-30: " To do this, the pattern of gene expression in the host stem cells for genes in the database of the present invention must be analyzed. A comparison is then made of the level of expression of the same genes, in the graft."
relevant	Page 3, lines 20-25: "Because the database contains many unknown and uncharacterized genes, an important use of the invention is to discover new genes that are relevant to hematopoiesis and stem cell growth. The database also has value because it could be mined for specific gene discovery, for example to find new genes that are surface markers (*e.g.* for flow cytometry), growth factors, or receptors for growth factors that regulate stem cell growth."

The examiner stated that "involved" in claim 19 was vague and indefinite because the examiner believed that the specification did not specify genes involved in hematopoeisis. Hematopoiesis refers to the formation and development of red and white blood cells from stem cells. *Kuby (1997), Immunology, 3rd Ed., pp 47-49.* On page 5, lines 23-27, the present specification discloses that one of the applications of the microchip is to identify and characterize genes that are relevant to hematopoiesis and stem cell growth and that the relevancy is based on the inclusion of the genes in the database. One of the factors that may determine if a gene is involved in hemotopoesis is its expression level in the hematopoetic tissue. The list of genes in Appendix A includes 595 genes that have a role in hematopoiesis (page 6, lines 12-13 of the

specification). For example, genes whose "cdna id" numbers designated 767183, 489208, 854284, and 292357 encode hematopoietic cell-specific Lyn substrate 1, Hematological and Neurological expressed sequence 1, hematopoietic protein 1, and hematopoietic RING finger protein 1 respectively, that are associated with hematopoiesis based on the gene name description (Appendix A of the present application). The list of genes disclosed in the application are expressed at moderate to high levels in the hematopoietic tissue and therefore presents a subset of genes from the human genome that may have a role in hematopoiesis. However, for clarity, the term "involved in" is amended to "relevant to".

The examiner stated that the term "gene therapy" does not have an art recognized meaning. However, at least one commonly accepted interpretation of gene therapy is as follows: an approach to preventing and/or treating a genetic deficiency in a cell by the addition of new DNA and its insertion into the genome (Griffiths *et al.*, *Modern Genetic Analysis*, NCBI Online Book Series). For example, introducing a gene to a cell to produce a specific missing protein is one mode of gene therapy. The specification (page 11, lines 5-6) disclose gene therapy as "Gene therapy is used to alter or replace defective genes or to enhance the expression of specific genes".

The examiner mentioned that a claim cannot refer to an appendix according to MPEP 608.01 (p). However, based on our analysis of the relevant sections of the MPEP, there is no indication that a reference to an appendix is prohibited in claims. If necessary, the applicants will amend the title "Appendix A" to "Table 4" and refer to Table 4 in claims 14-15. In addition, the sequences for the GenBank accession numbers listed in Appendix A are publicly available.

> The specification **need not disclose what is well-known** to those skilled in the art and **preferably omits that which is well-known** to those skilled and already available to the public. *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987); and *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1463, 221 USPQ 481, 489 (Fed. Cir. 1984). (*emphasis added*).

If the GenBank accession numbers are known, obtaining their corresponding nucleotide or amino acid sequences is well known in the art.

V. Claims 12-22 are Enabled

The term "related" is deleted from claim 13.

Nucleotide sequences for the genes, ESTs, and cDNAs listed in Appendix A are publicly available in the GenBank and the respective GenBank accession numbers were provided in Appendix A. Therefore, based on the disclosure of the present application, a person of ordinary skill in the art can obtain a microarray as disclosed herein.

Constructing microchips are routine in the art when identification of DNA molecules and their sequences are publicly available. Several scientific literature illustrate the construction of microarrays and applications of microarray data.

> Xiang and Chen (2000) cDNA microarray technology and its applications. *Biotechnol Adv.* 18(1):35-46. Review.
>
> Brown PO, Botstein D. (1999)Exploring the new world of the genome with DNA microarrays. *Nat Genet.* 21(1 Suppl):33-7. Review.

Contrary to examiner's belief, constructing microarrays either in house or through commercial sources is routine in the art.

VI. Research Genetics Gene Filters do not Anticipate Claims 12-22

The Research Genetics gene filters that the applicants used to identify the genes expressed in hematopoietic tissue contained several thousands of cDNAs and ESTs from a UniGene database, with no preference as to their expression profiles. The nucleotide segments in the Research Genetics filters represented a random subset of cDNAs and ESTs from the entire human genome. In contrast, a microchip of the present disclosure includes a specific collection of genes, ESTs, and cDNAs that are expressed at moderate to high levels in hematopoietic tissue.

> A claim is anticipated only **if each and every element as set forth** in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).
>
> The identical invention must be **shown in as complete detail as is contained in the claim**. *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). (*emphasis added*)

The Research Genetics Filters do not describe a specific collection of molecules in a microarray as set forth in claims 12-22 that are expressed in hematopoietic tissue. Therefore, Research Genetics gene filters do not anticipate claims 12-22.

Applicants request the examiner to allow the pending claims.

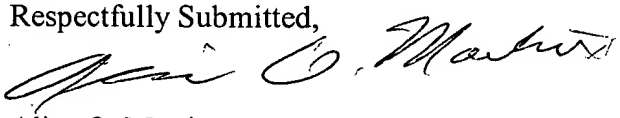
VII. Other Issues

A copy of the abstract of the Xiang and Chen (2000) reference and a print out of the website (www.image.llnl.gov) sent previously as part of an IDS, are resubmitted along with this paper as requested. A print out of the web link ftp.resgen.com/pub/genefilters cannot be located.

Applicants' representative requests a telephone interview with the examiner prior to issuance of another Office Action.

No other fees are believed due at this time, however, please charge any deficiencies or credit any over payments to deposit account number 12-0913 with reference to our attorney docket no (21726/92526).

Respectfully Submitted,



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1: Biotechnol Adv. 2000 Mar;18(1):35-46. Related Articles, Lin

ELSEVIER FULL-TEXT ARTICLE

cDNA microarray technology and its applications.

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The cDNA microarray is the most powerful tool for studying gene expressio in many different organisms. It has been successfully applied to the simultaneous expression of many thousands of genes and to large-scale gene discovery, as well as polymorphism screening and mapping of genomic DNA clones. It is a high throughput, highly parallel RNA expression assay technique that permits quantitative analysis of RNAs transcribed from both known and unknown genes. This technique provides diagnostic fingerprints by comparing gene expression patterns in normal and pathological cells, and because it can simultaneously track expression levels of many genes, it provides a source of operational context for inference and predication about complex cell control systems. This review describes this recently developed cDNA microarray technology and its application to gene discovery and expression, and to diagnostics for certain diseases.

PMID: 14538118 [PubMed]

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The I.M.A.G.E. Consortium can provide custom arraying and rearraying services for public EST projects; please contact **image@image.llnl.gov** to discuss details.

Read an editorial in The Scientist about the I.M.A.G.E. Consortium (February 15, 1999).

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